respectfully traverses the rejection. It appears that the Examiner has several different concerns. Applicant will attempt to address them in turn.

As explained in the specification, there is currently considerable interest in the "antioxidant" properties of foods and nutraceuticals. There is considerable evidence of the beneficial properties of "antioxidant" nutrients towards health. It has been presumed that these benefits stem from the antioxidant actions or from the free radical trapping actions (or from both) of these substances. However, the exact source of the benefits is not known. Assuming that the benefits are coming from the antioxidant properties, many tests have been developed to measure these properties. A number of the more popular tests are briefly discussed in the Background section of the present application. These tests tend to suffer from complexity or toxicity of ingredients or both. However, these tests have been used to measure antioxidants in foods and other nutrients (nutraceuticals), and there appears to be some correlation between substance with high measured "antioxidant" levels and beneficial results upon ingestion of the substances.

However, it is not clear exactly how one should go about measuring "antioxidants". At the simplest level an antioxidant is a reducing substance. That is, theory suggests that various cellular components become oxidized resulting in cellular damage. However, if a reducing agent is present, the component will be rapidly reduced (thus avoiding cellular damage) and/or the reducing agent will protect the cellular component. Thus, many of the current antioxidant tests, the current invention included, operate by measuring the amount of reducing material present in a test sample. That is, the tests operate on the basis of a redox or oxidation-reduction reaction. Typically, an oxidant reacts with and oxidizes the test substance. (The reducing material in the test substance is oxidized and the oxidant is reduced). The amount of remaining oxidant (or the reduced oxidant) is quantified allowing a measurement of the unknown reducing

substances in the test substance. As pointed out in the specification, any oxidant can be used, but the redox potential of the oxidant will effect the types of reducing agents measured. For example, iodine has a less positive redox potential than bromine, which is used in some antioxidant tests. As a result there are some reducing agents that are more negative than bromine but not more negative than iodine. These reducing agents would not be measured by the present test. However, it appears that the majority of naturally occurring antioxidants in foods and nutraceuticals do not fall into this group since published bromine-based measurements generally track the measurements produced by the present test.

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The Examiner states "it is unclear whether the concentrations as measured in these samples indicate the level of *just antioxidants or the level of total generally oxidizable constituents* within the sample" (emphasis added). The point is that antioxidants and generally oxidizable substance are one and the same thing. Because of the way that "antioxidants" is defined, redox reactions with amino acids or any other material is not a concern. Any substance that is oxidized by iodine is, by definition, an antioxidant. In fact, cysteine (mentioned by Alexander) is generally thought of as an antioxidant.

support? 16.

Alexander also mentions a number of items which I doubt are antioxidants

The Examiner is also concerned that besides oxidation iodine can cause iodination of many organics substances such as oleic acid or tyrosine. In the tests described by Alexander, iodination or oxidation were both measured by determining the **disappearance of iodine**. In the present test oxidation is measured by the **appearance of iodide ions**. In an oxidation reaction the iodine molecule extracts an electron from a reducing substance and becomes converted into **iodide**. However, in iodination the iodine molecule interacts with the substance being iodinated and becomes covalently bound to that substance. That is, the iodinated substance shares an electron with iodine to form a covalent bond. There is no oxidation/reduction and **iodide does not appear**.

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?! Summary, line 1

Thus, there is no reason to worry about iodination reactions. Potentially, if there was a tremendous excess of material that could be iodinated over reducing material, the reactive iodine might become exhausted before the oxidation/reduction was complete. However, this is not a worry for at least two reasons. First, iodinations are generally slow compared to redox reactions. Therefore, even with an excess of material that can be iodinated, the redox reaction would generally occur before the iodine was used up. More importantly, the present test uses a tremendous excess of iodine to sample so that the reactive iodine cannot become exhausted in practice (see page 7).

my problem is not calibration per se but the absence of any confirmation of what is being measured

Applicant respectfully takes difference with the Examiner's comments concerning need for calibration. Applicant has explained how the readings are corrected for any iodide present in the reagent (top of page 9). In actual practice the samples are also corrected for presence of iodide in the test sample before the start of the test. Such corrections would be obvious to any person of ordinary skill in the art. It is mentioned on page 11 that vitamin C reacts very rapidly with iodine (this is also confirmed in Alexander). In theory one could make a calibration curve, but this appears without benefit because vitamin C is quantitatively oxidized so that IRU (corrected iodide measurements) correlate directly with vitamin C or other rapidly acting reducing agents. The present test simply provides comparative values indicating the amount of antioxidants (reducing agents) present in a sample. It is not clear what benefit one would gain by expressing these figures in terms of known amount of vitamin C or some other calibrating substance. Applicant is not aware of any rule that requires calibration to ensure patentability. The present measurements are useful to indicate that a first sample of a test material has a higher or lower level of antioxidant as compared to a second sample of a test material.

Finally, Applicants respectfully disagree with the Examiner's statements concerning enablement relative to antioxidants. The chemical structures of all of the antioxidants in foods and nutraceuticals are presently unknown. Nevertheless, people consume these materials and obtain benefits from them. It is perfectly acceptable to demonstrate an invention by example. There is no known chemical reason why the current invention should not detect all antioxidants with redox potentials more negative than that of the iodine/iodide pair. As demonstrated in Alexander, polymers of oxidizable materials may tend to oxidize more slowly. Therefore, a graphic showing iodine reduction as a function of time may be useful with the present invention as some samples may have more slow acting compounds than other samples. Total iodine reduction units can be determined by allowing the reaction to go essentially to completion; however, the time for completion may be different for different materials. The Examiner will appreciate that useful comparative measurements can be obtained by giving the iodine reducing units after a known period of time (say 60 min). If the same test is applied to two different samples, and one of the samples shows twice the reduction of iodine after 60 min, it can be concluded that the samples are significantly different. This comparison is most useful where both samples are supposedly of the same material. For example, if this difference were found with two samples of grape juice, one would conclude that either the concentration of grape was quite different (something that can be checked by measuring other constituents of the juice) or that the antioxidant content of one of the samples was quite different—perhaps exhausted by previous oxidative challenge.

Applicant also traverses the rejections under 35 U.S.C. § 112, first paragraph. Since several different antioxidant tests are already in use, those skilled in the art have little problem in adopting a new test. Several parties are presently investigating the use of the test. Contrary to the Examiner's assertions there appear to be no major drawbacks in employing the test. The test appears

just as likely to measure reducing substances (within the proper oxidation-reduction range) as any other redox-based test. Those of skill realize any potential shortcomings of redox tests.

In summary, the present test measures reduction of iodine to iodide. Unlike the test described by Alexander, which measured disappearance of iodine, the present test is not confounded by iodination. Covalent addition of iodine to a compound does not produce iodide and is not measured by the present test. Applicant is not aware of any common antioxidant nutrients that are not detected by the present test. All experiments to date have indicated that common antioxidant nutrients are detected. The test is functional and useful. The specification gives sufficient instructions for one of ordinary skill to practice the invention. If the Examiner has specific objections to the scope of the claims, Applicant would be please to address them.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (213) 337-6700 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,

HOGAN & HARTSON L.L.P.

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By: Stefan J. Kirchanski

Stefan J. Kirchanski
Registration No. 36,568
Attorney for Applicant(s)

500 South Grand Avenue, Suite 1900
Los Angeles, California 90071
Phone: 213-337-6700
Fax: 213-337-6701